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10/591,824	09/06/2006	Juliana C.N. Chan	INSIG1.017APC	3083

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EXAMINER	
PANDE, SUCHIRA	
ART UNIT	**PAPER NUMBER**
1637	

NOTIFICATION DATE	DELIVERY MODE
07/21/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com
eOAPilot@kmob.com

Office Action Summary	Application No.	Applicant(s)	
	10/591,824	CHAN ET AL.	
	Examiner	Art Unit	
	SUCHIRA PANDE	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-24* is/are pending in the application.

4a) Of the above claim(s) *8-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/6/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group I invention (claims 1-8) in the reply filed on May 15, 2009 is acknowledged. The traversal is on the ground(s) that applicant has deleted the reference to TNF-α from claim 17. Hence art cited by Examiner to demonstrate Lack of Unity namely Nakamura et al. that taught the primers for TNF-α amplification is no longer applicable. This is not found persuasive because amended claim 17 recites :

"A kit for detecting a Chinese diabetic, subject at risk for developing, a nephropathy comprising: primers for amplifying the ACE and ALR2 genes ; and instructional material teaching how to determine whether the subject is at risk for developing the nephropathy."

Prior art teaches primers for amplifying ACE gene (see abstract of O'Dell et al. (1995) Br. Heart J. vol. 73: 368-371 where primers ACE1, ACE2 and ACE3 are taught for ACE gene amplification)

Prior art also teaches primers for amplifying ALR2 gene (see Hodgkinson et al. (2001) Kidney international Vol. 60: pp 211-218 where on page 213 col. 1 par. 2 where one sense and two different antisense primers for amplifying ALR2 are taught).

Thus prior art teaches primers for amplifying the ACE and ALR2 genes. Hodgkinson et al. also teach use of Kit format for packaging products (see page 213 par. 3 where MAXIscript system of Ambion is taught).

As shown above all the components of the kit recited in claim 17 are taught to one of ordinary skill in the art by prior art. Thus at the time of the invention prior art taught primers and kit for amplifying ACE and ALR2 genes. The preamble of instant claim recites intended use and does not further limit the product namely primers taught by prior art.

Hence prior art taught the product of claim 17 to one of ordinary skill in the art at the time the invention was made. Therefore the kit and primers for amplifying ACE and ALR2 genes lacks the same or corresponding special technical features as the method of group I invention.

Therefore, the requirement is still deemed proper and is therefore made FINAL.

Applicant has also elected following species for examination:

a. Method for detecting a diabetic subject of Chinese decent :

ii. at risk for developing a nephropathy

Gene / Sequence Restriction Subgroups

b. Applicant has amended the base claim 1 to require presence of an I/D genotype of an ACE gene; z-2 genotype of an ALR2 gene; and a C106T genotype of an ALR2 gene. Hence in view of the amended claim language of the base claim, the pending claim 1 will be examined to the extent it read upon the above 3 genotypes.

c. Applicant has elected ALR2 gene from the genes recited for amplification by PCR. Hence newly added claims that refer to non elected AGT and TNF-α genes are withdrawn from consideration.

d. Applicant has amended claim 4 to require detection of two genes ACE and ALR2. Hence the relevant primers for ACE gene (SEQ ID NOs. 1&2) and the relevant primers for ALR2 gene for the elected allele z-2 (SEQ ID NOs: 7&8); the minimum number of primers required for the amplification of the two genes recited will be examined in this action.

2. Newly added claims 19 and 23 and amended dependent claim 8 drawn to method are directed to non elected genes namely AGT and TNF-α genes, hence these claims are being withdrawn from consideration.

2. Commensurate with above elections, claims 8-24 drawn to non elected genes or product (array and kit) are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on May 15, 2009. Currently claims 1 and 3-7 drawn to method are active and will be examined in this application.

Priority

3. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). Instant application is national stage of PCT/CN2005/000508 filed on April 15, 2005. Applicant claims priority to CN 200410033864.X filed on 15 April 2004, however no certified English translation of above Chinese document has been received. Hence for application of prior art the priority of instant application is considered to be the filing date of above PCT application i.e. April 15, 2005.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on 9/6/2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Specification

5. Page 8 par. 0045 contains a typographical error. In line two of this par. “Tape” should read "Type". Appropriate correction is required.

Claim Interpretation

6. The phrase “subject of Chinese descent” is not defined and no guidance is provided as to how one can identify such humans. For purposes of applying art Examiner is broadly interpreting the claim to read upon any piece of prior art that refers to human diabetic population.

Claim Rejections - 35 USC § 112

7. Claims 1, 3-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term “subject of Chinese descent" in claim 1 is a relative term which renders the claim indefinite. The term “subject of Chinese descent" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree by having which a human being will qualify to be a “subject of Chinese descent", and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Examiner is unclear if Applicant is referring to a specific genetic make up while referring to “subject of

Chinese descent" if so then what is it? The specification as filed does not provide any definition or criteria to be used in order to distinguish “subject of Chinese descent" from other human subjects. Hence Examiner does not know the method of claims 1 and 3-7 is applicable to which population of human subjects and how to identify that subset to which this method applies. Appropriate correction is required.

Claim Objections

8. Claims 1, 4 and 5 are objected to because of the following informalities: Only acronyms ACE and ALR2 have been used to identify the recited genes in above three claims. These acronyms in claims 1, 4 and 5 should be preceded by the full form to recite.

---Angiotensin Converting Enzyme (ACE) gene----

---Aldose Reductase (ALR2) gene---

Appropriate correction is required.

Claim Rejections - 35 USC § 103

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of

35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1, 3-4, 6 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (2002) Diabet. Med. Vol. 19: pp 113-118; Marre et al. (1997) J. Clin. Invest. vol. 99 No 7: pp 1585-1595 and Neamat-Allah et al. (2001) Diabet. Med. vol. 18; pp 906-914.

Regarding claim 1, Liu et al. teach a method for detecting a diabetic subject of Chinese descent at risk for developing a nephropathy (see page 113 abstract),

comprising the step of determining whether a sample from the subject polymorphic sequences comprising a (z-2) genotype of an ALR2 gene 5'-(CA) repeats (see page 113 methods where detection of polymorphism using PCR is taught. See page 114 Introduction par. 1 where an (AC)n dinucleotide repeat polymorphism in the promoter region of the ALR2 gene has been shown to be associated with nephropathy in Type I diabetes is taught);

wherein the presence of the polymorphic sequence indicates that the subject is at risk for developing the nephropathy (see page 115 Discussion where z-2 allele when present together with any other alleles other than z+2 (allele X), found to be an independent risk factor for diabetic nephropathy, thus Liu et al. teach polymorphic sequences comprising a (z-2) genotype of an ALR2 gene 5'-(CA) repeats wherein the presence of the polymorphic sequence indicates that the subject is at risk for developing the nephropathy).

Regarding claim 3, Liu et al. teach wherein the sample is blood (see page 114 section genomic DNA preparation and analysis where blood is taught as sample).

Regarding claim 4, Liu et al. teach further comprising the step of amplifying the ALR2 gene (see page 114 par. 4 where PCR amplification of ALR2 is taught).

Regarding claim 6, Liu et al. teach wherein the subject is at risk for developing, Type 2 diabetes (see page 113 par. 1 abstract).

Regarding claim 1, Liu et al. do not teach:

an I/D genotype of an ACE gene;

a C106T genotype of an ALR2 gene in the promoter region,

Regarding claim 1, Marre et al. teach an I/D genotype of an ACE gene (see page 1585 Abstract where an I/D genotype of an ACE gene is taught).

Regarding claim 7, Marre et al. teach wherein the I/D genotype comprises a DD genotype (see page 1585 par. 1 where subjects with ACE DD genotype are taught).

Regarding claim 4, Marre et al. teach further comprising the step of amplifying the ACE gene (see page 1587 par. 1 where nested PCR amplification of ACE gene is taught).

Regarding claim 1, Neamat-Allah et al. teach a C106T genotype of an ALR2 gene polymorphism in the promoter region (see page 907 col. 1 par. 4 last part where ALR2-106 (C/T) polymorphism in the promoter region is taught to be associated with diabetic nephropathy).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to practice the method of Marr et al. and Neamat-Allah et al. in the method of Liu et al. The motivation to do so is provided to one of ordinary skill by teachings of Marre et al.; Neamat-Allah et al. and Liu et al.

Marre et al. state “diabetic nephropathy is a glomerular disease due to uncontrolled diabetes and genetic factors. It can be caused by glomerular hypertension produced by capillary vasodilation, due to diabetes, against constitutional glomerular resistance. As angiotensin II increases glomerular pressure, we studied the relationship between genetic polymorphisms in the renin-angiotensin system-angiotensin I converting enzyme (ACE)------and the renal involvement of insulin dependent diabetic subjects----:those exposed to the risk of nephropathy due to diabetes” (see page 1582 abstract). They go on to conclude "The severity of renal involvement was associated with ACE insertion /deletion (I/D) polymorphism".

Neamat-Allah et al. state “Meta-analyses provide more convincing evidence of a role for the ALR2-106 marker than for the microsatellite marker in diabetic nephropathy (DN). More studies are now required to confirm these results and to establish whether the ALR2-106 polymorphism has a functional role in DN” (see page 906 section conclusions).

Thus based on these above combined teachings one of ordinary skill in the art knows that all the three polymorphisms namely I/D genotype of an ACE gene; a (z-2) genotype of an ALR2 gene 5'-(CA) repeats and a C106T genotype

of an ALR2 gene in the promoter region are implicated in development of renal nephropathy in diabetic subject. Since each genotype contributes towards development of diabetic nephropathy in diabetic subjects therefore, one of ordinary skill in the art has a reasonable expectation to expect that detection of a combination of two or more of these polymorphisms in a human will make that diabetic human being even more susceptible to developing diabetic nephropathy than other diabetics who lack these specific polymorphisms.

11. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al.; Marre et al. and Neamat-Allah et al. as applied to claim 4 above further in view of Norberg et al. (US pat. 6197505 B1 issued March 2001); Ko et al. (1995) Diabetes 44 (7), 727-732 and Buck et al. (1999) BioTechniques 27: 528-536.

Regarding claim 5, Liu et al.; Marre et al. and Neamat-Allah et al. teach method of claim 4 above. Liu et al.; Marre et al. and Neamat-Allah et al. teach PCR amplification of ACE And ALR2 gene but do not teach wherein the amplifying step is performed with primers having SEQ ID NO. 1 and SEQ ID NO. 2 for the I/D genotype of the ACE gene, SEQ ID NO. 7 and SEQ ID NO. 8 for a (z-2) genotype of the ALR2 gene, or SEQ ID NO. 9 and SEQ ID NO. 10 for a C106T genotype of the ALR2 gene in the promoter region.

Regarding claim 5, Norberg et al. teach primers having SEQ ID NO. 1 and SEQ ID NO. 2 for the I/D genotype of the ACE gene. See alignment below

SEQ ID NO 1

```
RESULT 1
AR137275
LOCUS       AR137275                 24 bp    DNA     linear   PAT 16-
JUN-2001
```

```
DEFINITION  Sequence 22 from patent US 6197505.
ACCESSION   AR137275
VERSION     AR137275.1  GI:14478784
KEYWORDS    .
SOURCE      Unknown.
  ORGANISM  Unknown.
            Unclassified.
REFERENCE   1  (bases 1 to 24)
  AUTHORS   Norberg,L.Torbjorn., Andersson,M.Kristina. and
            Lindstrom,P.Harry.Rutger.
  TITLE     Methods for assessing cardiovascular status and
compositions for
            use thereof
  JOURNAL   Patent: US 6197505-A 22 06-MAR-2001;
FEATURES             Location/Qualifiers
     source          1. .24
                     /organism="unknown"
                     /mol_type="unassigned DNA"
ORIGIN

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  Best Local Similarity   100.0%;  Pred. No. 2.1;
  Matches   24;  Conservative    0;  Mismatches    0;  Indels    0;
Gaps    0;

Qy          1 CTGGAGACCACTCCCATCCTTTCT 24 SEQ ID NO 1
              ||||||||||||||||||||||||
Db          1 CTGGAGACCACTCCCATCCTTTCT 24 Sequence 22
```

SEQ ID NO: 2

```
RESULT 1
AR137276
LOCUS       AR137276                 25 bp    DNA     linear   PAT 16-
JUN-2001
DEFINITION  Sequence 23 from patent US 6197505.
ACCESSION   AR137276
VERSION     AR137276.1  GI:14478785
KEYWORDS    .
SOURCE      Unknown.
  ORGANISM  Unknown.
            Unclassified.
REFERENCE   1  (bases 1 to 25)
  AUTHORS   Norberg,L.Torbjorn., Andersson,M.Kristina. and
            Lindstrom,P.Harry.Rutger.
  TITLE     Methods for assessing cardiovascular status and
compositions for
            use thereof
  JOURNAL   Patent: US 6197505-A 23 06-MAR-2001;
FEATURES             Location/Qualifiers
     source          1. .25
                     /organism="unknown"
                     /mol_type="unassigned DNA"
ORIGIN
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  Matches   25;  Conservative    0;  Mismatches    0;  Indels    0;
Gaps    0;

Qy          1 GATGTGGCCATCACATTCGTCAGAT 25
              |||||||||||||||||||||||||
Db          1 GATGTGGCCATCACATTCGTCAGAT 25
```

Thus SEQ ID NO: 1 of instant claim is 100 % identical to amplification primer of Sequence 22 taught by Norberg et al. (see Table 2) and SEQ ID NO: 2 of instant claim is 100 % identical to amplification primer of Sequence 23 taught by Norberg et al. (see Table 2). Both these primers are for amplification of ACE gene.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to choose the desired primers for ACE gene from the primers of ACE gene that are taught by Norberg et al. in the method of Liu et al.; Marre et al. and Neamat-Allah et al.

See Art Recognized Equivalence for the Same Purpose SEE MPEP 2144.06 Art Recognized Equivalence for the Same Purpose [R-6] < SUBSTITUTING EQUIVALENTS KNOWN FOR THE SAME PURPOSE. In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982).

One of ordinary skill in the art is capable of choosing the desired primer combination to suit their particular requirement from the repertoire of ACE primers taught by Norberg et al.

Regarding claim 5, Ko et al. teach primers having SEQ ID NO. 7 and SEQ ID NO. 8 for a (z-2) genotype of the ALR2 gene. See alignment below

SEQ ID NO: 7

```
RESULT 3
HSU72619/c
LOCUS       HSU72619                3350 bp    DNA     linear   PRI 02-
JUL-1997
DEFINITION  Human aldose reductase gene, promoter region.
ACCESSION   U72619
VERSION     U72619.1  GI:2228537
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata;
Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates;
Haplorrhini;
            Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 3350)
  AUTHORS   Ko,B.C., Lam,K.S., Wat,N.M. and Chung,S.S.
  TITLE     An (A-C)n dinucleotide repeat polymorphic marker at the 5'
end of
            the aldose reductase gene is associated with early-onset
diabetic
            retinopathy in NIDDM patients
  JOURNAL   Diabetes 44 (7), 727-732 (1995)
   PUBMED   7789640
REFERENCE   2  (bases 1 to 3350)
  AUTHORS   Ko,B.C. and Chung,S.S.
  TITLE     Identification and characterization of multiple osmotic
respnse
            sequences in the aldose reductase gene
  JOURNAL   J. Biol. Chem. 272 (1997) In press
REFERENCE   3  (bases 1 to 3350)
  AUTHORS   Ko,B.C.B.
  TITLE     Direct Submission
  JOURNAL   Submitted (26-SEP-1996) The Institute of Molecular Biology,
The
            University of Hong Kong, 8 Sassoon Road, Pokfulam, Hong
Kong
FEATURES             Location/Qualifiers
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                     /mol_type="genomic DNA"
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                     /map="7q35"
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     repeat_region   645. .690
                     /rpt_type=tandem
                     /rpt_unit_seq="gt"
     misc_feature    1498. .1630
                     /note="osmotic response sequence"
     mRNA            2732. .>2837
                     /product="aldose reductase"
     exon            2732. .2837
                     /number=1
     CDS             2772. .>2837
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                     /product="aldose reductase"
                     /protein_id="AAB61992.1"
                     /db_xref="GI:2228538"
                     /translation="MASRLLLNNGAKMPILGLGTWK"
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ORIGIN

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Gaps    0;

Qy          1 GAATCTTAACATGCTCTGAACC 22
              ||||||||||||||||||||||
Db        763 GAATCTTAACATGCTCTGAACC 742
```

SEQ ID NO: 8

```
RESULT 5
HSU72619
LOCUS       HSU72619                3350 bp    DNA     linear   PRI 02-
JUL-1997
DEFINITION  Human aldose reductase gene, promoter region.
ACCESSION   U72619
VERSION     U72619.1  GI:2228537
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata;
Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates;
Haplorrhini;
            Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 3350)
```

```
  AUTHORS   Ko,B.C., Lam,K.S., Wat,N.M. and Chung,S.S.
  TITLE     An (A-C)n dinucleotide repeat polymorphic marker at the 5'
end of
            the aldose reductase gene is associated with early-onset
diabetic
            retinopathy in NIDDM patients
  JOURNAL   Diabetes 44 (7), 727-732 (1995)
   PUBMED   7789640
REFERENCE   2  (bases 1 to 3350)
  AUTHORS   Ko,B.C. and Chung,S.S.
  TITLE     Identification and characterization of multiple osmotic
respnse
            sequences in the aldose reductase gene
  JOURNAL   J. Biol. Chem. 272 (1997) In press
REFERENCE   3  (bases 1 to 3350)
  AUTHORS   Ko,B.C.B.
  TITLE     Direct Submission
  JOURNAL   Submitted (26-SEP-1996) The Institute of Molecular Biology,
The
            University of Hong Kong, 8 Sassoon Road, Pokfulam, Hong
Kong
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                     /rpt_unit_seq="gt"
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     exon            2732. .2837
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                     /product="aldose reductase"
                     /protein_id="AAB61992.1"
                     /db_xref="GI:2228538"
                     /translation="MASRLLLNNGAKMPILGLGTWK"
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ORIGIN

  Query Match             100.0%;  Score 19;  DB 5;  Length 3350;
  Best Local Similarity   100.0%;  Pred. No. 1.6e+02;
  Matches   19;  Conservative    0;  Mismatches    0;  Indels    0;
Gaps    0;

Qy          1 GCCCAGCCCTATACCTAGT 19
```

```
                ||||||||||||||||||
Db        626 GCCCAGCCCTATACCTAGT 644
```

Thus SEQ ID NO: 7 of instant claim is 100 % identical to nt at location 762 to 742 from sequence of ALR2 accession no U72619 deposited in Genebank by Ko et al. Further SEQ ID NO: 8 of instant claim is 100 % identical to nt at location 626 to 644 from sequence of ALR2 accession no U72619 deposited in Genebank by Ko et al.

Thus sequence of accession no U72619 comprises the sequences recited as primers of SEQ ID NO 7 and 8 in instant application.

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have used the sequences of ALR2 gene taught by Ko et al. in the method of Liu et al.; Marre et al. and Neamat-Allah et al. to design the **primers** claimed in instant application as SEQ ID No 7 and 8 for (z-2) genotype of the ALR2 gene detection.

In the recent court decision *KSR International Co. v. Teleflex Inc., 82* 127 SCt 1727 (2007), the U.S. Supreme Court determined that if the combination of the claimed elements was "obvious to try" by a person of ordinary skill, this might show that such a combination was obvious under §103. Regarding "obvious to try", the Court stated:

"A person of ordinary skill is also a person of ordinary creativity, not an automaton.
The same constricted analysis led the Court of Appeals to conclude, in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was "obvious to try." Id., at 289 (internal quotation marks omitted). When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If

this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103."

The sequence of ALR2 gene/region is taught to one of ordinary skill by prior art and one of ordinary skill in the art is capable of designing primers useful for amplifying a given region of any nucleic acid whose sequence is known and detecting it using suitable technique. PCR amplification is currently one of the fastest, cheapest way of detecting presence of any given nucleic acid, provided some information is available based on which amplification primers flanking the region to be amplified can be designed.

Since the claimed primers simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers of the ALR2 gene/region and concerning which a biochemist of ordinary skill would attempt to obtain suitable primers flanking the region of interest, the claimed primers are *prima facie* obvious over the cited references in the absence of secondary considerations.

Buck expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer

ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

Conclusion

12. All claims under consideration 1 and 3-7 are rejected over prior art.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUCHIRA PANDE whose telephone number is (571)272-9052. The examiner can normally be reached on 8:30 am -5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Suchira Pande
Examiner
Art Unit 1637

/Suchira Pande/
Examiner, Art Unit 1637